

WHAT IS CLAIMED IS:

1. A purified ACT-4 receptor polypeptide that comprises at least five contiguous amino acids from an amino acid sequence shown in Fig. 5.
2. The polypeptide of claim 1 that exhibits at least eighty percent sequence identity to the amino acid sequence of Fig. 5.
3. The polypeptide of claim 2 having an antigenic determinant common to a protein comprising the amino acid sequence shown in Fig. 5.
4. The polypeptide of claim 3 that is a full-length polypeptide.
5. The polypeptide of claim 4 comprising a domain selected from a group of domains consisting of a signal sequence, an intracellular domain, a transmembrane domain, and an extracellular domain.
6. The polypeptide of claim 5 that comprises an extracellular domain.
7. The polypeptide of claim 6, wherein said extracellular domain comprises an intrachain loop formed by disulfide bonding of two cysteine residues.
8. The polypeptide of claim 7, wherein said extracellular domain comprises three intrachain loops, each formed by disulfide bonding of two cysteine residues.
9. The polypeptide of claim 8, wherein said polypeptide is present on the surface of activated CD4⁺ T-cells, and is substantially absent on activated CD8⁺ T cells and resting T-cells.

10. The polypeptide of claim 9 that is naturally occurring.

11. The polypeptide of claim 10 that is human.

12. The polypeptide of claim 11 that has a molecular weight of about 50 kDa before deglycosylation and about 27 kDa thereafter.

13. The polypeptide of claim 12 comprising the amino acid sequence of Fig. 5.

14. An extracellular domain of a polypeptide of claim 3.

15. The extracellular domain of claim 14 comprising an intrachain loop formed by disulfide bonding of two cysteine residues.

16. The extracellular domain of claim 15 comprising three intrachain loops, each formed by disulfide bonding of two cysteine residues.

17. The extracellular domain of claim 16 that is soluble.

18. The extracellular domain of claim 17 that is capable of specifically binding to an ACT-4 ligand.

19. The extracellular domain of claim 18 that is immunogenic.

20. The extracellular domain of claim 19 that competes with an ACT-4-h-1 receptor polypeptide for specific binding to an antibody.

21. The extracellular domain of claim 20 that is fused to a second polypeptide.

093345 05404
000000 5482560

22. The extracellular domain of claim 21, wherein the second polypeptide is a constant region of an immunoglobulin heavy chain.

23. A polypeptide consisting essentially of an epitope specifically bound by an antibody designated L106.

24. An antibody that specifically binds to an ACT-4-h-1 receptor polypeptide.

25. The antibody of claim 24 that is a monoclonal antibody.

26. The antibody of claim 25 that inhibits activation of CD4⁺ T-cells.

27. The monoclonal antibody of claim 25 that stimulates activation of CD4⁺ T-cells.

28. The antibody of claim 25 that competes with an antibody designated L106 for specific binding to an ACT-4-h-1 receptor polypeptide.

29. The antibody of claim 25 that competes with an antibody designated L106 for specific binding to activated CD4⁺ T-cells.

30. The antibody of claim 25 that is fused to a coat protein of a filamentous phage.

31. The antibody of claim 29 that is L106.

32. A humanized antibody comprising a humanized heavy chain and a humanized light chain:

(1) the humanized light chain comprising three complementarity determining regions (CDR1, CDR2 and CDR3) having amino acid sequences from the corresponding complementarity determining regions of a L106 antibody light

TOP SECRET 54225360

chain, and having a variable region framework sequence substantially identical to a human light chain variable region framework sequence; and

(2) the humanized heavy chain comprising three complementarity determining regions (CDR1, CDR2 and CDR3) having amino acid sequences from the corresponding complementarity determining regions of a L106 antibody heavy chain, and having a variable region framework sequence substantially identical to a human heavy chain variable region framework sequence;

wherein the humanized antibody specifically binds to an ACT-4-h-1 receptor polypeptide with a binding affinity that is within three-fold of the binding affinity of a L106 antibody.

33. An immunotoxin comprising the antibody of claim 31 fused to a toxin polypeptide.

34. The antibody of claim 25 that specifically binds to a different epitope on an ACT-4-h-1 receptor polypeptide than that specifically bound by an L106 antibody.

35. A fragment of the antibody of claim 31 that specifically binds to an ACT-4-h-1 receptor polypeptide.

36. A hybridoma producing antibody L106, said hybridoma deposited as ATCC__.

37. A method of screening an antibody for specific binding to the same epitope as that bound by an L106 antibody, said method comprising:

providing a solution comprising an antibody to be screened, said L106 antibody, and an ACT-4-h-1 receptor polypeptide, said polypeptide specifically binding to said L106 antibody; and

measuring specific binding between said polypeptide and said L106 antibody, or between said polypeptide and said antibody to be screened, to indicate whether said antibody to

TOP SECRET 054103

be screened reacts with the same epitope as said L106 antibody.

38. A method of localizing an epitope specifically bound by an L106 antibody, said method comprising:

providing a family of ACT-4-h-1 receptor polypeptides, each member of said family comprising a contiguous segment of at least four amino acids; and

measuring specific binding between a polypeptide from said family and said L106 antibody to indicate the presence of said epitope within said polypeptide.

39. A nucleic acid fragment encoding a heavy chain of an antibody of claim 31.

40. A nucleic acid fragment encoding a light chain of an antibody of claim 31.

41. A nucleic acid fragment encoding an ACT-4 polypeptide of claim 1.

42. The nucleic acid fragment of claim 41 that exhibits at least eighty percent sequence identity with the nucleic acid sequence shown in Fig. 5.

43. The nucleic acid fragment of claim 42 that encodes a full-length ACT-4 polypeptide.

44. The nucleic acid fragment of claim 43 comprising the translated region of the nucleic acid sequence shown in Fig. 5.

45. An isolated cell line containing a nucleic acid fragment of claim 41.

46. The isolated cell line of claim 45, wherein the ACT-4 receptor polypeptide is expressed on the surface of said cell.

09852845-051101
FOI 54325860

48. The isolated cell line of claim 47, wherein said nucleic acid fragment is incorporated in the genome of said cell line.

50. A method of screening for immunosuppressive agents, said method comprising:

- contacting an ACT-4-h-1 receptor polypeptide with a potential immunosuppressive agent; and
- detecting specific binding between said ACT-4-h-1 receptor polypeptide and said agent, said specific binding indicative of immunosuppressive activity.

52. A method for screening for an ACT-4 ligand, said method comprising:

- contacting a biological sample containing said ACT-4 ligand with an ACT-4-h-1 receptor polypeptide;
- isolating a complex formed between said ligand and said ACT-4-h-1 receptor polypeptide; and
- dissociating said complex to obtain said ligand.

54. A method of inducing an immune response to a selected antigen comprising:

administering a monoclonal antibody of claim 27 to a patient; and
exposing said patient to said selected antigen.

55. A method of detecting activated CD4⁺ T-cells, said method comprising:

contacting a tissue sample from a patient with a monoclonal antibody of claim 24 and

detecting specific binding between said monoclonal antibody and said tissue sample to reveal the presence of said activated CD4⁺ T-cells.

56. The method of claim 55, wherein the presence of activated T-cells revealed by said specific binding is diagnostic of a disease or condition of the immune system.

57. A pharmaceutical composition comprising a monoclonal antibody of claim 26 and a pharmaceutically acceptable excipient.

58. An ACT-4 ligand that specifically binds to an ACT-4-h-1 receptor polypeptide.

095345-004
TOTTENHAM